Application No.: 10/606,969

Office Action Dated: November 15, 2006

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. (Canceled)

2. (Currently Amended) An injectable depot composition comprising:

(a) a low molecular weight bioerodible, biocompatible polymer;

(b) a solvent selected from the group consisting of aromatic alcohols, esters of aromatic acids, aromatic ketones, and mixtures thereof, said solvent having miscibility in

aromatic acids, aromatic ketolics, and mixtures thereof, said solvent having miscromity in

water of less than or equal to 7% at 25°C, and present in an amount effective to plasticize the

polymer and form a gel therewith; and

(c) a beneficial agent;

wherein said composition is selected to deliver the beneficial agent in a controlled manner

over a duration of less than about seven days.

Claims 3-6 (Canceled).

7. (Currently Amended) The injectable depot composition of claim 2, wherein the

solvent is a mixture of an aromatic alcohol and an ester of an aromatic acid.

8. (Original) The injectable depot composition of claim 7, wherein the aromatic alcohol

is benzyl alcohol and the ester of an aromatic acid is a lower alkyl ester or an aralkyl ester of

benzoic acid.

9. (Original) The injectable depot composition of claim 8, wherein the ester of an

aromatic acid is benzyl benzoate and the lower alkyl ester of an aromatic acid is ethyl

benzoate.

10. (Currently Amended) The injectable depot composition of claim 1 or claim 2 wherein

the low molecular weight polymer has a molecular weight ranging from about 3000 to about

10,000.

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11. (Currently Amended) The injectable depot composition of claim 2 [[10]], wherein the low molecular weight polymer has a molecular weight ranging from about 3000 to about 8,000.

- 12. (Currently Amended) The injectable depot composition of claim 2 [[10]], wherein the low molecular weight polymer has a molecular weight ranging from about 4000 to about 6,000.
- 13. (Currently Amended) The injectable depot composition of claim $\underline{2}$ [[10]], wherein the low molecular weight polymer has a molecular weight of about 5000.
- 14. (Currently Amended) The injectable depot composition of elaim 1 or claim 2, wherein the polymer is selected from the group consisting of a polylactide[[s]], polyglycolide[[s]], polyamhydride[[s]], polyamine[[s]], polyesteramide[[s]], polyorthoester[[s]], polydioxanone[[s]], polyacetal[[s]], polyketal[[s]], polycarbonate[[s]], polyphosphoester[[s]], polyorthocarbonate[[s]], polyphosphazene[[s]], succinate[[s]], poly(malic acid), poly(amino acid[[s]]), polyvinylpyrrolidone, polyethylene glycol, polyhydroxycellulose, chitin, chitosan, hylauronic acid and or a copolymer[[s]], terpolymer[[s]] and or mixture[[s]] thereof.
- 15. (Currently Amended) The injectable depot composition of claim 1 or claim 2, wherein the polymer is a lactic acid-based polymer.
- 16. (Original) The injectable depot composition of claim 15, wherein the polymer is a copolymer of lactic acid and glycolic acid.
- 17. (Currently Amended) The injectable depot composition of claim 2 [[15]] comprising about 5 wt.% to about 90 wt.% of the [[a]] biodegradable, biocompatible lactic acid-based polymer and wherein the polymer is a lactic acid-based polymer having a weight average molecular weight in the range of about 3,000 to about 10,000.

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18. (Currently Amended) The injectable depot composition of claim 2 [[17]], wherein the polymer comprises represents about 10 wt.% to about 85 wt.% of the composition.

- 19. (Currently Amended) The injectable depot composition of claim 2 [[18]], wherein the polymer comprises represents about 35 wt.% to about 65 wt.% of the composition.
- 20. (Currently Amended) The injectable depot composition of elaim 1 or claim 2, further including at least one of the following: a pore former; a solubility modulator for the beneficial agent; and an osmotic agent.
- 21. (Currently Amended) The injectable depot composition of elaim 1 or claim 2 wherein the beneficial agent is selected from a drug, protein[[s]], enzyme[[s]], hormone[[s]], polynucleotide[[s]], nucleoprotein[[s]], polysaccharide[[s]], glycoprotein[[s]], lipoprotein[[s]], polypeptide[[s]], steroid[[s]], analgesic[[s]], local anesthetic[[s]], antibiotic agent[[s]], chemotherapeutic agent[[s]], immunosuppressive agent[[s]], anti-inflammatory agent[[s]], antiproliferative agent[[s]], antimitotic agent[[s]], angiogenic agent[[s]], antipsychotic agent[[s]], central nervous system (CNS) agent[[s]], anticoagulant[[s]], fibrinolytic agent[[s]], growth factor[[s]], antibody[[ies]], or ocular drug[[s]], and metabolites, analogs, derivatives, and fragments thereof.
- 22. (Currently Amended) The injectable depot composition of claim 2 [[21]] wherein the beneficial agent is selected from an analgesic[[s]], local anesthetic[[s]], antibiotic agent[[s]], anti-inflammatory agent[[s]], antipsychotic agent[[s]], or anticoagulant[[s]], and metabolites, analogs, derivatives, and fragments thereof.
- 23. (Currently Amended) The injectable depot composition of claim 2 [[21]] wherein the beneficial agent is present in an amount of from 0.1 to 50% by weight of the combined amounts of the polymer, the solvent and the beneficial agent.

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24. (Currently Amended) The injectable depot composition of claim $\underline{2}$ [[21]] wherein the beneficial agent is in the form of particles dispersed or dissolved in the gel.

- 25. (Currently Amended) The injectable depot composition of claim 24 wherein the beneficial agent is in the form of particles <u>have having</u> an average particle size of from 0.1 to 250 microns.
- 26. (Currently Amended) The injectable depot composition of claim 24 wherein the beneficial agent is in the form of particles wherein the particles further comprise[[s]] a component selected from the group consisting of a stabilizing agent, bulking agent, chelating agent and a buffering agent.

Claims 27-28 (Canceled).

- 29. (Currently Amended) An injectable depot composition comprising:
- (a) approximately 5 wt.% to approximately 90 wt.% of a low molecular weight biodegradable, biocompatible lactic acid-based polymer having a weight average molecular weight in the range of approximately 1,000 to approximately 10,000;
- (b) a solvent selected from the group consisting of an aromatic alcohol, an ester of an aromatic acid, and mixtures thereof, said solvent having miscibility in water of less than or equal to 7% at 25°C, and present in an amount effective to plasticize the polymer and form a gel therewith, wherein the aromatic alcohol has the structural formula (I)

in which Ar is a substituted or unsubstituted aryl or heteroaryl group, n is zero or 1, and L is a linking moiety; and

(c) a beneficial agent;

wherein said composition is selected to deliver the beneficial agent in a controlled manner over a duration less than about seven days.

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30. (Currently Amended) The injectable depot composition of <u>claim any one of claims</u> 27, 28 or 29 wherein the <u>low molecular weight lactic acid-based polymer has a molecular weight ranging from about 3000 to about 10,000.</u>

- 31. (Currently Amended) The injectable depot composition of claim <u>29</u> [[30]], wherein the <u>low molecular weight lactic acid-based</u> polymer has a molecular weight ranging from about 3000 to about 8,000.
- 32. (Currently Amended) The injectable depot composition of claim <u>29</u> [[30]], wherein the <u>low molecular weight lactic acid-based polymer has a molecular weight ranging from about 4000 to about 6,000.</u>
- 33. (Currently Amended) The injectable depot composition of claim <u>29</u> [[30]], wherein the <u>low molecular weight lactic acid-based polymer has a molecular weight of about 5000.</u>
- (Currently Amended) The injectable depot composition of any one of claims 27, 28 or claim 29, wherein the polymer is selected from the group consisting of a polylactide[[s]], polyglycolide[[s]], polyanhydride[[s]], polyamine[[s]], polyesteramide[[s]], polyorthoester[[s]], polydioxanone[[s]], polyacetal[[s]], polyketal[[s]], polycarbonate[[s]], polyphosphoester[[s]], polyorthocarbonate[[s]], polyphosphazene[[s]], succinate[[s]], poly(malic acid), poly(amino acid[[s]]), polyvinylpyrrolidone, polyethylene glycol, polyhydroxycellulose, chitin, chitosan, hylauronic acid and or a copolymer[[s]], terpolymer[[s]] and or mixture[[s]] thereof.
- 35. (Canceled).
- 36. (Currently Amended) The injectable depot composition of claim <u>29</u> [[35]], wherein the <u>lactic acid-based</u> polymer is a copolymer of lactic acid and glycolic acid.
- 37. (Canceled).

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38. (Currently Amended) The injectable depot composition of claim <u>29</u> [[37]], wherein

the <u>lactic acid-based</u> polymer represents <u>comprises</u> about 10 wt.% to about 85 wt.% of the

composition.

39. (Currently Amended) The injectable depot composition of claim <u>29</u> [[38]], wherein

the <u>lactic acid-based</u> polymer represents <u>comprises</u> about 35 wt.% to about 65 wt.% of the

composition.

Claims 40-43. (Canceled).

44. (Currently Amended) The injectable depot composition of claim 29, wherein the

solvent is a mixture of an aromatic alcohol and an ester of an aromatic acid.

45. (Original) The injectable depot composition of claim 44, wherein the aromatic alcohol

is benzyl alcohol and the ester of an aromatic acid is a lower alkyl ester or an aralkyl ester of

benzoic acid.

46. (Original) The injectable depot composition of claim 45, wherein the ester of an

aromatic acid is benzyl benzoate and the lower alkyl ester of an aromatic acid is ethyl

benzoate.

47. (Original) The injectable depot composition of claim 44, wherein the ratio of the

aromatic alcohol to the ester of an aromatic acid is in the range of about 1% to about 99% by

weight.

48. (Currently Amended) The injectable depot composition of claim 44 [[47]], wherein

the ratio of the aromatic alcohol to the ester of an aromatic acid is in the range of about 20%

to about 80% by weight.

49. (Currently Amended) The injectable depot composition of claim 45 comprising about

5 wt.% to about 90 wt.% of a biodegradable, biocompatible wherein the lactic acid-based

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polymer <u>has</u> having a weight average molecular weight in the range of about 3,000 to about 10,000.

- 50. (Currently Amended) The injectable depot composition of <u>claim any one of claims</u> 27, 28 or 29, further including at least one of the following: a pore former; a solubility modulator for the beneficial agent; and an osmotic agent.
- (Currently Amended) The injectable depot composition of any one of claim 27, 28 or 29 wherein the beneficial agent is selected from a drug, protein[[s]], enzyme[[s]], hormone[[s]], polynucleotide[[s]], nucleoprotein[[s]], polysaccharide[[s]], glycoprotein[[s]], lipoprotein[[s]], polypeptide[[s]], steroid[[s]], analgesic[[s]], local anesthetic[[s]], antibiotic agent[[s]], chemotherapeutic agent[[s]], immunosuppressive agent[[s]], anti-inflammatory agent[[s]], antiproliferative agent[[s]], antimitotic agent[[s]], angiogenic agent[[s]], antipsychotic agent[[s]], central nervous system (CNS) agent[[s]], anticoagulant[[s]], fibrinolytic agent[[s]], growth factor[[s]], antibody[[ies]], or ocular drug[[s]], and metabolites, analogs, derivatives, and fragments thereof.
- 52. (Currently Amended) The injectable depot composition of claim <u>29</u> [[51]] wherein the beneficial agent is selected from <u>an</u> analgesic[[s]], local anesthetic[[s]], antibiotic agent[[s]], anti-inflammatory agent[[s]], antipsychotic agent[[s]], <u>or an</u> anticoagulant[[s]], <u>and</u> metabolites, analogs, derivatives, and fragments thereof.
- 53. (Currently Amended) The injectable depot composition of claim <u>29</u> [[51]] wherein the beneficial agent is present in an amount of from 0.1 to 50% by weight of the combined amounts of the polymer, the solvent and the beneficial agent.
- 54. (Currently Amended) The injectable depot composition of claim <u>29</u> [[51]] wherein the beneficial agent is in the form of particles dispersed or dissolved in the gel.
- 55. (Currently Amended) The injectable depot composition of claim 54 wherein the beneficial agent is in the form of particles have having an average particle size of from 0.1 to Page 9 of 19

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250 microns.

56. (Currently Amended) The injectable depot composition of claim 54 wherein the beneficial agent is in the form of particles wherein the particle further comprise[[s]] a component selected from the group consisting of a stabilizing agent, bulking agent, chelating agent and a buffering agent.

Claims 57-58 (Canceled).

- 59. (Currently Amended) An injectable depot composition comprising:
- (a) approximately 5 wt.% to approximately 90 wt.% of a low molecular weight poly(lactide-co-glycolide) (PLGA) copolymer having a weight average molecular weight in the range of approximately 3,000 to approximately 10,000;
- (b) approximately 5 wt.% to approximately 90 wt.% of a solvent selected from the group consisting of an aromatic alcohol, an ester of an aromatic acid, and mixtures thereof, said solvent having miscibility in water of less than or equal to 7% at 25°C, and present in an amount effective to plasticize the polymer and form a gel therewith; and
- (c) a beneficial agent; wherein said composition is selected to deliver the beneficial agent in a controlled manner over a duration of less than about seven days.
- 60. (Original) The injectable depot composition of claim 59, wherein the aromatic alcohol is benzyl alcohol and the ester of an aromatic acid is benzyl benzoate.

Claims 61-104 (Canceled).

- 105. (Original) A kit for administration of a beneficial agent to a subject comprising:
 - (a) a low molecular weight bioerodible, biocompatible polymer;
- (b) a solvent selected from the group consisting of aromatic alcohols, esters of aromatic acids, aromatic ketones, and mixtures thereof, said solvent having miscibility in

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water of less than or equal to 7% at 25°C, and present in an amount effective to plasticize the polymer and form a gel therewith; and

- (c) a beneficial agent; and optionally, one or more of the following:
- (d) an emulsifying agent;
- (e) a pore former;
- (f) a solubility modulator for the beneficial agent, optionally associated with the beneficial agent; and
 - (g) an osmotic agent;

wherein at least the beneficial agent, optionally associated with the solubility modulator, is maintained separated from the solvent until the time of administration of the beneficial agent to a subject.

- 106. (New) The injectable depot composition of claim 2, wherein the polymer is a polylactide, polyglycolide, or a copolymer, terpolymer or mixture thereof.
- 107. (New) The injectable depot composition of claim 2 wherein the solvent is an aromatic alcohol.
- 108. (New) The injectable depot composition of claim 107 wherein the aromatic alcohol is benzyl alcohol.
- 109. (New) The injectable depot composition of claim 2 wherein the solvent is an ester of an aromatic acid.
- 110. (New) The injectable depot composition of claim 109 wherein the ester of an aromatic acid is a lower alkyl ester or an aralkyl ester of benzoic acid.
- 111. (New) The injectable depot composition of claim 110 wherein the lower alkyl ester is ethyl benzoate and the aralkyl ester is benzyl benzoate.
- 112. (New) The injectable depot composition of claim 2 wherein the polymer comprises about 5 wt.% to about 90 wt.% of the composition.
- 113. (New) The injectable depot composition of claim 17 wherein the lactic acid-based polymer is a copolymer of lactic acid and glycolic acid.

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114. (New) The injectable depot composition of claim 17 wherein the lactic acid-based polymer comprises about 10 wt.% to about 85 wt.% of the composition.

- 115. (New) The injectable depot composition of claim 17 wherein the lactic acid-based polymer comprises about 35 wt.% to about 65 wt.% of the composition.
- 116. (New) The injectable depot composition of claim 29, wherein the polymer is a polylactide, polyglycolide, or copolymer, terpolymer or mixture thereof.
- 117. (New) The injectable depot composition of claim 29 wherein the solvent is an aromatic alcohol.
- 118. (New) The injectable depot composition of claim 117 wherein the aromatic alcohol is benzyl alcohol.
- 119. (New) The injectable depot composition of claim 29 wherein the solvent is an ester of an aromatic acid.
- 120. (New) The injectable depot composition of claim 119 wherein the ester of an aromatic acid is a lower alkyl ester or an aralkyl ester of benzoic acid.
- 121. (New) The injectable depot composition of claim 120 wherein the lower alkyl ester is ethyl benzoate and the aralkyl ester is benzyl benzoate.